General

Guideline Title

ACR Appropriateness Criteria® non-invasive clinical staging of bronchogenic carcinoma.

Bibliographic Source(s)

Ravenel JG, Mohammed TH, Rosenzweig KE, Ginsburg ME, Kanne JP, Kestin LL, Kirsch J, Parker JA, Rimner A, Saleh AG, Expert Panels on Thoracic Imaging and Radiation Oncologyâ€“Lung. ACR Appropriateness CriteriaÂ® non-invasive clinical staging of bronchogenic carcinoma. [online publication]. Reston (VA): American College of Radiology (ACR); 2013. 11 p. [68 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Ravenel JG, Mohammed TH, Movsas B, Ginsburg ME, Kirsch J, Kong FM, Parker JA, Reddy GP, Rosenzweig KE, Saleh AG, Expert Panel on Thoracic Imaging and Radiation-Oncology-Lung. ACR Appropriateness Criteria® non-invasive clinical staging of bronchogenic carcinoma. [online publication]. Reston (VA): American College of Radiology (ACR); 2010. 11 p.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Non-invasive Clinical Staging of Bronchogenic Carcinoma

Variant 1: Non–small-cell lung carcinoma.

Radiologic Procedure	Rating	Comments	RRL*
CT chest without contrast	9	Through adrenal glands.	☢☢☢
CT chest with contrast	9	Through adrenal glands. See text. There are pros and cons to the use of IV contrast. There is no strong scientific evidence to support the use of IV contrast.	☢☢☢
FDG-PET/CT skull base to mid-thigh	9	If a diagnostic chest CT has not yet been performed, obtain FDG-PET skull base to mid-thigh and CT chest with or without contrast. Can omit for staging pure ground glass neoplasms.	☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation
MRI chest without and with contrast	1	Usually not appropriate for present or asymptomatic with adenocarcinoma histology greater than 3 cm in	0

Radiologic Procedure	Rating	Comments	RRL*
		size or mediastinal adenopathy. See statement regarding contrast in text below under "Anticipated Exceptions."	
MRI head without contrast	5	If gadolinium contraindicated.	O
X-ray chest	5	May be useful as a baseline comparison to help detect complications of therapy and other non-tumor related disease in follow-up.	☢
CT abdomen with contrast	5		☢☢☢
CT head with contrast	5	If MRI is contraindicated and neurological symptoms are present.	☢☢☢
Tc-99m bone scan whole body	5	Not necessary if PET has been done.	☢☢☢
CT head without contrast	3		☢☢☢
MRI chest without and with contrast	3	Useful for evaluating chest wall invasion, cardiac invasion, and for local staging of superior sulcus tumors.	O
MRI chest without contrast	2	Useful for evaluating chest wall invasion, cardiac invasion, and for local staging of superior sulcus tumors. If gadolinium contraindicated.	O
CT abdomen without contrast	1		☢☢☢
CT abdomen without and with contrast	1		☢☢☢☢
CT head without and with contrast	1		☢☢☢
CT chest without and with contrast	1	Through adrenal glands.	☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: Small-cell lung carcinoma.

Radiologic Procedure	Rating	Comments	RRL*
CT chest and abdomen with contrast	9		☢☢☢☢
MRI head without and with contrast	9	See statement regarding contrast in text below under "Anticipated Exceptions."	O
FDG-PET/CT skull base to mid-thigh	8	If a diagnostic chest CT has not yet been performed, obtain FDG-PET skull base to mid-thigh and CT chest with contrast.	☢☢☢☢
CT chest and abdomen without contrast	5	Use this procedure if contraindication to contrast. Also, consider MRI of abdomen instead of unenhanced CT of abdomen.	☢☢☢☢
MRI head without contrast	5	If gadolinium contraindicated.	O
X-ray chest	5	May be useful as a baseline comparison to help detect complications of therapy and other non-tumor related disease in follow-up.	☢
CT head with contrast	5	If MRI contraindicated and neurological symptoms are present.	☢☢☢
Tc-99m bone scan whole body	5	Not necessary if FDG-PET/CT has been performed.	☢☢☢
CT head without contrast	2		☢☢☢
MRI chest without and with contrast	2		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative**

Radiologic Procedure	Rating	Comments	RRL*
MRI chest without contrast	2		☢☢☢
CT head without and with contrast	1		☢☢☢
CT chest and abdomen without and with contrast	1		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Non–small-cell Lung Carcinoma

Staging

Staging of any tumor is done to determine the extent of disease. Staging information is important for two reasons: to determine prognosis and to select patients for surgical intervention and/or a different modality. The TNM staging system is widely used to classify lung tumors. In 2007 it was revised after epidemiologic evidence demonstrated differences in survival of several tumor features that warranted reclassification. In the TNM classification, "T" indicates the features of the primary tumor, "N" indicates metastasis to regional lymph nodes, and "M" refers to the presence or absence of distant metastases. The most recent revision was performed by the International Association for the Study of Lung Cancer (IASLC).

The current IASLC 7th edition classification consist of 4 stages. Stage I has been divided into 2 groups: IA and IB. Data have consistently shown a better outcome for patients with stage IA disease — that is, T1N0M0 — than for any other subset. Median survival time is 59 months for stage 1A compared with 48 months for stage 1B. Stage IB is defined as patients with T2a tumors. Stage II is also subdivided into A and B groups. Median survival time for patients with stage IIA disease — that is, T1 or T2a lesions with involved hilar nodes or T2b lesions without hilar nodes — is higher than for those with stage IIB disease (T2bN1M0 or T3N0M0).

Stage III is divided into IIIA and IIIB, where IIIB is considered unresectable disease (i.e., T4 and/or N3). In the current classification, tumors >7 cm or with invasion of the chest wall (T3) are considered to be potentially resectable in the absence of mediastinal adenopathy and provided that vital structures in the mediastinum, such as the great vessels, heart, and aerodigestive tract, are not involved. Satellite nodules in the same lobe are now considered T3 as well. The designation T4 is reserved for lesions with extensive invasion of a vertebral body, trachea, esophagus, heart, or great vessels, as well as tumors with satellite tumor nodule(s) within the ipsilateral nonprimary-tumor lobe of the lung. In the current system, patients with ipsilateral mediastinal and subcarinal nodal metastasis (N2) are also considered to have resectable cancer, although a benefit of surgery over definitive chemoradiotherapy has been difficult to prove. For the most part, only patients with single-station ipsilateral mediastinal nodal disease fall into the potentially operable category. The N3 category refers to metastasis in the contralateral mediastinal, hilar, scalene, or supraclavicular lymph nodes. N3 disease is considered to be unresectable. While T4 tumors are generally said to be unresectable, selected T4N0M0 tumors may be considered for operation when there is limited involvement of a vertebral body, mediastinal fat, superior vena cava, or left atrium. In the current classification, stage IV includes patients with evidence of distant metastasis (M1), malignant nodules in the contralateral lung, pleural nodules, and malignant pleural or pericardial effusion.

A number of imaging modalities have been used in staging lung cancer. These have included standard and conventional tomography as well as computed tomography (CT), magnetic resonance imaging (MRI), and fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET). In all cases histologic confirmation of the tumor is mandatory, and in most cases the histologic proof should be confirmed for the lesion that established the highest stage of disease (an exception would be clear-cut evidence of multiple sites of metastatic disease). Any potential solitary metastatic lesion must be confirmed histologically prior to deeming a patient unresectable.

Chest Radiographs

The vast majority of primary lung cancers are initially detected on routine chest radiographs; however, there is little need for the chest radiograph when a tumor has been detected incidentally on CT examination performed for other purposes.

Computed Tomography

CT is the major imaging modality of choice in the initial evaluation of patients with suspected bronchogenic carcinoma. Numerous studies have shown that its value in staging is limited, because there are no morphologic criteria that would allow distinction between benign and malignant lymph nodes, but it does provide the anatomic basis to determine the most appropriate steps for diagnosis and management.

Traditionally, chest CT for staging of lung cancer is extended into the abdomen to include the adrenal glands. Whether this requires intravenous contrast material is debatable and has not been definitively addressed. For some the addition of contrast improves evaluation of the mediastinum. While it would appear advantageous to have contrast enhancement of the liver, it is rarely the sole site of disease at diagnosis and often visible with liver windows. At the same time unenhanced CT has the advantage of definitively characterizing incidental adrenal nodules. Much of this debate has been rendered moot by the use of FDG-PET/CT, and thus the use of intravenous contrast should be based on patient factors and the discretion of the interpreting radiologist.

Evaluation of Primary Tumor (the T Factor)

Computed Tomography

The distinction between T1 and T2 lesions is generally based on size and rarely impacts the choice of therapy. Imaging cannot reliably determine the presence of visceral pleural invasion for peripheral tumors. Confirming T3 or T4 status based on imaging alone, however, can be quite difficult. Features such as discrete bone destruction, rib erosion, or tumor adjacent to a mediastinal structure without associated fat plane are diagnostic of chest wall or mediastinal invasion. CT features of chest wall invasion include: >3 cm of contact with the pleural surface, pleural thickening, absent fat planes, and obtuse angle of tumor with the chest wall.

The specificity of any of these signs is relatively poor, as pleural reaction and inflammation may mimic neoplastic involvement, and localized chest pain remains a much more specific determinant of invasion. Using thin collimation with coronal and sagittal reformation improves accuracy for both chest wall and mediastinal invasion. In the absence of definitive signs of invasion, surgery may be necessary to confirm or exclude direct invasion.

Magnetic Resonance Imaging

MRI can aid in problem solving and is superior to CT for detecting involvement of the neural foramina, spinal canal, and brachial plexus in superior sulcus tumors. Surgery is contraindicated by local extension if the brachial plexus is involved above the level of T1, if more than 50% of a vertebral body is invaded, or if there is invasion of the trachea or esophagus. Invasion of the subclavian, common carotid and vertebral arteries, less than 50% vertebral body invasion, and extension into the neural foramina should be considered relative contraindications to surgery. MRI can be useful in excluding chest wall involvement. When using cine MRI during free breathing, a finding of sliding between the tumor and mediastinum or chest wall has been shown to be diagnostic of lack of invasion. The converse, however, is not necessarily indicative of invasion, as adhesion and local inflammatory changes may also restrict tumor motion.

Evaluation of Nodal Metastasis (the N Factor)

Computed Tomography

Because size is the main criteria for malignancy, CT is a rather inaccurate modality for staging the mediastinum. A lymph node >1 cm in short-axis diameter is generally considered "positive." While there is no lower threshold that guarantees freedom from disease, the overall chance that a node harbors malignancy is influenced by size. For example, the prevalence of metastatic disease in lymph nodes is approximately 30% for nodes 10 to 15 mm in diameter and 67% for nodes >15 mm in diameter. Among 43 studies conducted from 1991–2005, the sensitivities of CT for nodal disease ranged from 26% to 86% and specificity ranged from 31% to 97%, and a pooled sensitivity and specificity from a total of 5,111 patients in whom the prevalence of nodal disease was 28% were 51% and 86%, respectively. CT does, however, provide anatomic relationships critical for interpreting FDG-PET studies and allows for selection of the most appropriate pathway for biopsy.

The location of the primary tumor has a strong and relatively predictable influence on the likely location of metastatic nodes. Right upper lobe tumors most often drain to right paratracheal nodes (2R and 4R), while right, middle and lower lobe tumors most frequently drain to lower right paratracheal and subcarinal nodes (4R and 7R). On the left the common sites for nodal metastases for the left upper lobe include AP window and prevascular nodes (5L and 6L) and prevascular and subcarinal (6L and 7L) for the left lower lobe. For lower lobe tumors the frequency of upper mediastinal lymph node involvement (levels 2, 4, 5, and 6) is greater for tumors in the superior segment (64%) versus basal segments (36%).

The preoperative detection of N2 disease generally renders a patient unsuitable for primary surgery treatment. Depending on the extent of N2 disease and other factors, patients may receive either neoadjuvant therapy in an attempt to clear the mediastinal disease prior to surgery or primary chemotherapy and radiation therapy with curative intent. The choice should be guided by histologic confirmation and an enlarged mediastinal lymph node alone by CT is insufficient to make a patient inoperable. While FDG-PET/CT is becoming the mainstay of preoperative staging (see below), if it is not performed and a negative CT alone is used, up to 30% of patients will eventually be shown to have positive mediastinal lymph nodes.

Magnetic Resonance Imaging

MRI is not typically used for mediastinal staging, although abnormal lymph nodes can be detected using this technique. A lack of standardization of protocols, however, makes comparison of results difficult.

Most protocols use a short-tau inversion recovery (STIR) sequence, and with it MRI may approach the accuracy of FDG-PET/CT for detecting nodal metastases. In another study, quantitative analysis of STIR images using a lymph node saline ratio was found to be more sensitive and specific compared to PET/CT. Studies using diffusion weighted sequences have mixed results. Overall, the number of studies and subjects is too small to determine if MRI has any relevant role in mediastinal staging.

Positron Emission Tomography/Computed Tomography

Integrated FDG-PET/CT imaging outperforms CT alone, FDG-PET alone, conventional visual correlation, or superimposition of CT and FDG-PET acquired individually. Pooling all FDG-PET studies (many without the CT component) resulted in a sensitivity of 74% and a specificity of 85% in 2,865 patients with a prevalence of mediastinal disease of 29%. In particular, specificity may be further degraded in areas endemic for granulomatous disease. Even when the results of CT and FDG-PET are negative, the false negative rate in the mediastinum ranges from 8% to 16%. Much of the reason for the large variance in studies is due to the lack of a reproducible cut-off for benign and malignant nodes across studies. Sensitivity is often enhanced when qualitative evaluation is used, whereas it tends to suffer when quantitative measures are used.

For lung neoplasms presenting as a pure ground glass nodule, there does not appear to be added benefit to adding FDG-PET/CT to the staging evaluation. For part-solid nodules the value of FDG-PET/CT is generally related to the size of the solid core and is suggested for part-solid nodules ≥8 mm. In a recent study of part solid nodules with >50% ground glass component, there were no true positive mediastinal nodes or distant disease detected by FDG-PET/CT. Further research is needed to determine whether the indication for FDG-PET/CT staging should be based on percentage of ground glass or absolute diameter of the solid core.

While FDG-PET is not an endpoint in the staging workup, FDG-PET scans can decrease the number of futile thoracotomies by 20%. The PLUS study randomized stage I–III patients who were potentially operable to FDG-PET or no PET and showed a reduction in the "futile" thoracotomy rate (thoracotomy performed in patients with unresectable disease) by 20% (41% without FDG-PET vs 21% with FDG-PET). This was confirmed in a randomized controlled trial where the addition of FDG-PET/CT to conventional staging reduced the rate of futile thoracotomies by 17% (52% without FDG-PET/CT compared to 35% with FDG-PET/CT). However, for clinical 1A patients, the yield of FDG-PET in preventing nontherapeutic pulmonary resection appears to be <10%. Thus, the ultimate success of FDG-PET in the mediastinum may be to spare advanced-stage patients extensive surgery.

It is clear that FDG-PET must be interpreted in the context of CT findings to maximize utility. The value of FDG-PET in staging the mediastinum depends on the CT findings. If the CT scan was positive by CT criteria, sensitivity increased to 100% and specificity decreased to 78%. In the setting of a negative CT scan, FDG-PET showed 82% sensitivity and 93% specificity. Modeling for size in combination with FDG-PET, the likelihood of malignancy in an FDG-PET negative node is 5% when the nose is 10 to 15 mm in diameter and 21% when it is >15 mm in diameter. Conversely, the likelihood of malignancy in an FDG-PET positive node is 62% when it is 10 to 15 mm in diameter and 90% when it is >15 mm in diameter. Moreover, the use of FDG-PET combined with CT can be critical in defining the most appropriate site for hilar and mediastinal lymph node biopsy.

For the FDG-PET negative mediastinum, there appear to be several caveats that can guide the decision about whether further mediastinal staging is necessary. A retrospective study of FDG-PET false negative results found that occult metastases were more likely to occur with increasing T-stage, central tumors, adenocarcinoma histology, and higher primary tumor standard uptake volume (SUV) (>6), although the actual number of false negative lymph nodes in this study was small (n=16). Other groups have found that in addition to these features, upper-lobe tumors and those with N1 positive disease also have a relatively high rate of occult disease in the mediastinum with histologic staging.

In summary, an FDG-PET negative mediastinum has an extremely high negative predictive value in small (T1a), peripheral tumors with a low primary tumor SUV and no significant activity in the hilar lymph nodes. Under these conditions it seems reasonable to proceed to surgery without prior pathological staging of the mediastinum.

Evaluation of Distant Metastasis (the M Factor)

Adrenal Glands

Adrenal nodules are a common incidental finding in the general population and in patients with lung cancer, but a density measurement of <10 Hounsfield units (HU) virtually assures the diagnosis of benign adenoma. If the measurement is >10 HU or if the initial study was performed with intravenous contrast, several techniques may be used to potentially rule in benignity. These include evaluating CT washout criteria, CT histogram analysis, MRI with in-phase and out-of-phase imaging, and FDG-PET/CT. While all these techniques can potentially rule in a benign lesion, their specificity is insufficient to rule in malignancy. Thus when the adrenal is the sole potential site of metastatic disease, biopsy is necessary to confirm its presence.

Liver

The liver is rarely the sole site of metastatic disease at time of diagnosis, occurring in approximately 3% of cases. As most chest CT scans will cover the majority of the liver, dedicated hepatic imaging is generally not indicated. While FDG-PET has not been formally evaluated for imaging of liver metastasis related to lung cancer, experience in other malignancies suggests that it can accurately detect liver metastases by focal uptake greater than the background of the liver. When findings are discordant or indeterminate, MRI and biopsy are appropriate strategies to evaluate liver lesions.

Bone

While bone scintigraphy is quite sensitive for detecting osseous metastases, the false positive rate approaches 40%. Since fewer than 5% of lung cancer patients have occult bone metastases at presentation, routine bone scintigraphy is probably not warranted. Several studies have shown FDG-PET to have a similar sensitivity and accuracy, with improved specificity and negative predictive value. Thus, if whole-body FDG-PET has already been performed, bone scintigraphy should be considered unnecessary.

Central Nervous System

In the absence of neurological symptoms, cerebral metastases are unusual, and the routine staging of subjects with a normal clinical examination yields positive findings in less than 10% of patients. Of the various histologic subtypes, adenocarcinoma and large-cell carcinoma are most frequently associated with asymptomatic cerebral metastases. Cerebral imaging is therefore used more effectively in patients with neurologic symptoms or prior to resection of T2 tumors or planned resection of IIIA disease.

Small-cell Lung Carcinoma (SCLC)

SCLC is an aggressive neoplasm of neuroendocrine cell origin with a distinct biologic behavior and is therefore grouped separately from other primary lung neoplasms. SCLC represents about 15% to 25% of all lung cancers and tends to occur in patients younger than those with the other lung cancers. SCLC mostly originates in the submucosa of proximal airways such as the lobar bronchi, or main bronchi, while a small percentage (<5%) originate in the peripheral areas of the lung. The tumor itself is highly cellular and has a limited fibrotic or inflammatory response. Consequently, the tumor spreads rapidly through the lymphatics and blood vessels at an early stage, resulting in early nodal and distant metastatic deposits. From a practical standpoint, SCLC may be thought of as a "systemic" disease at the time of diagnosis.

Historically, SCLC was stratified by a 2-stage system as defined by the IASLC. The first stage included patients with the disease restricted to one hemithorax with regional lymph node metastases, including ipsilateral hilar, ipsilateral and contralateral mediastinal, ipsilateral and contralateral supraclavicular, and ipsilateral pleural effusion independent of cytology. The second stage comprised patients with more extensive disease. The practical effect of this was to divide patients into one of two treatment groups, chemotherapy and radiotherapy for limited disease and chemotherapy alone for extensive disease. Based on further analysis of resected small-cell carcinomas, the IASLC has found sufficient prognostic variability using the TNM system to warrant replacing the previous staging system. For surgically resected SCLC (n=349), there is a marked survival enhancement (>2 years) for both stage T1a and N0 cases compared with other surgically resected SCLCs. Moreover, the 5-year survival rate for resected stage I tumors is 57%. The overall 5-year survival rate for all surgically resected "limited disease" is 34.5%, compared to the 12% to 25% for traditional chemoradiotherapy.

CT is generally the first study performed in the evaluation of suspected SCLC on chest radiograph. The use of intravenous contrast may be helpful in evaluating the extent of disease and the relationship to mediastinal vascular structures. Although this will not necessarily change the staging, it may help determine the need for palliative radiation therapy in patients with distant metastatic disease. When metastatic disease is present, abdominal organs are involved in up to 60% of cases, with the adrenal gland and liver as the most frequent sites of disease. Because of this high frequency, a dedicated CT of the abdomen with contrast should also be obtained as part of routine staging.

FDG-PET/CT is often helpful during the staging process. Its main value lies in its ability to upstage patients with extensive disease to stage II and thus spare them from unnecessary therapy. Studies have shown that FDG-PET/CT results in a stage shift of up to 17% of cases. In prospective series this results in approximately 8% of subjects upstaged by the detection of metastatic disease when compared to traditional staging. Additionally, detection of additional involved nodes may allow for the appropriate adjustment of the radiation therapy plan in up to 25% of cases.

Due to the high incidence of brain metastases, routine imaging of the central nervous system (CNS) is warranted. Cerebral metastases have been said to be present in up to 10% of individuals at the time of diagnosis.

Bone is considered to be the most common site of metastatic disease overall (35% of cases), and therefore bone scintigraphy has generally been part of the initial staging evaluation. Bone scintigraphy can be omitted from staging when FDG-PET/CT is performed.

Summary

- For non–small-cell lung cancer, minimum staging should include a CT scan of the thorax and FDG-PET.

- Imaging of the CNS should be performed in symptomatic and high risk cases of non–small-cell lung cancer.
- For small-cell lung cancer staging should consist of CT of the chest and abdomen, FDG-PET, and imaging of the CNS; preferably with MRI.
- Histologic confirmation of the highest radiologic stage is appropriate particularly for single site suspected nodal or extra-thoracic disease.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (i.e., <30 mL/min/1.73 m^2), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73 m^2. For more information, please see the American College of Radiology (ACR) Manual on Contrast Media (see the "Availability of Companion Documents" field).

Abbreviations

- CT, computed tomography
- FDG-PET, fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography
- IV, intravenous
- MRI, magnetic resonance imaging
- PET, positron emission tomography
- Tc, technetium

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Bronchogenic carcinoma

- Non–small-cell lung carcinoma
- Small-cell lung carcinoma

Guideline Category

Diagnosis

Evaluation

Clinical Specialty

Internal Medicine

Nuclear Medicine

Oncology

Pathology

Pulmonary Medicine

Radiation Oncology

Radiology

Thoracic Surgery

Intended Users

Health Plans

Hospitals

Managed Care Organizations

Physicians

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of initial radiologic examinations for non-invasive clinical staging of patients with bronchogenic carcinoma

Target Population

Patients with bronchogenic carcinoma

Interventions and Practices Considered

1. X-ray chest
2. Computed tomography (CT)
    - Chest with contrast (through adrenal glands)
    - Chest without contrast (through adrenal glands)
    - Chest without and with contrast (through adrenal glands)
    - Chest and abdomen with contrast
    - Chest and abdomen without contrast
    - Chest and abdomen without and with contrast
    - Abdomen with contrast
    - Abdomen without contrast

- Abdomen without and with contrast
- Head with contrast
- Head without contrast
- Head without and with contrast

3. Magnetic resonance imaging (MRI)
    - Head without and with contrast
    - Head without contrast
    - Chest without and with contrast
    - Chest without contrast
4. Fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET)/CT skull base to mid-thigh
5. Technetium (Tc)-99m bone scan whole body

Major Outcomes Considered

- Utility of radiologic examinations in non-invasive clinical staging of bronchogenic carcinoma
- Survival time/rate

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Procedure

Staff will search in PubMed only for peer reviewed medical literature for routine searches. Any article or guideline may be used by the author in the narrative but those materials may have been identified outside of the routine literature search process.

The Medline literature search is based on keywords provided by the topic author. The two general classes of keywords are those related to the condition (e.g., ankle pain, fever) and those that describe the diagnostic or therapeutic intervention of interest (e.g., mammography, MRI).

The search terms and parameters are manipulated to produce the most relevant, current evidence to address the American College of Radiology Appropriateness Criteria (ACR AC) topic being reviewed or developed. Combining the clinical conditions and diagnostic modalities or therapeutic procedures narrows the search to be relevant to the topic. Exploding the term "diagnostic imaging" captures relevant results for diagnostic topics.

The following criteria/limits are used in the searches.

1. Articles that have abstracts available and are concerned with humans.
2. Restrict the search to the year prior to the last topic update or in some cases the author of the topic may specify which year range to use in the search. For new topics, the year range is restricted to the last 10 years unless the topic author provides other instructions.
3. May restrict the search to Adults only or Pediatrics only.
4. Articles consisting of only summaries or case reports are often excluded from final results.

The search strategy may be revised to improve the output as needed.

Number of Source Documents

The total number of source documents identified as the result of the literature search is not known.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Strength of Evidence Key

Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis and results.

Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.

Category 3 - The conclusions of the study may be valid but the evidence supporting the conclusions is inconclusive or equivocal.

Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author drafts or revises the narrative text summarizing the evidence found in the literature. American College of Radiology (ACR) staff draft an evidence table based on the analysis of the selected literature. These tables rate the strength of the evidence (study quality) for each article included in the narrative text.

The expert panel reviews the narrative text, evidence table, and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the table. Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The appropriateness ratings for each of the procedures included in the Appropriateness Criteria topics are determined using a modified Delphi methodology. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. American College of Radiology (ACR) staff distribute surveys to the panelists along with the evidence table and narrative. Each panelist interprets the available evidence and rates each procedure. The surveys are completed by panelists without consulting other panelists. The appropriateness rating scale is an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate"; 4, 5, or 6 are in the category "may be appropriate"; and 7, 8, or 9 are in the category "usually appropriate." Each panel member assigns one rating for each procedure for a clinical scenario. The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating.

If consensus is reached, the median rating is assigned as the panel's final recommendation/rating. Consensus is defined as eighty percent (80%) agreement within a rating category. A maximum of three rounds may be conducted to reach consensus. Consensus among the panel members must be achieved to determine the final rating for each procedure.

If consensus is not reached, the panel is convened by conference call. The strengths and weaknesses of each imaging procedure that has not reached consensus are discussed and a final rating is proposed. If the panelists on the call agree, the rating is proposed as the panel's consensus. The document is circulated to all the panelists to make the final determination. If consensus cannot be reached on the call or when the document is circulated, "No consensus" appears in the rating column and the reasons for this decision are added to the comment sections.

This modified Delphi method enables each panelist to express individual interpretations of the evidence and his or her expert opinion without excessive influence from fellow panelists in a simple, standardized and economical process. A more detailed explanation of the complete process can be found in additional methodology documents found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current literature and expert panel consensus.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Selection of appropriate radiologic imaging procedures for non-invasive clinical staging evaluation of patients with bronchogenic carcinoma

Potential Harms

- Even when the results of computed tomography (CT) and fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) are negative, the false negative rate in the mediastinum ranges from 8% to 16%.
- While bone scintigraphy is quite sensitive for detecting osseous metastases, the false positive rate approaches 40%.

Gadolinium-based Contrast Agents

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequela to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (i.e., <30

mL/min/1.73 m^2), and almost never in other patients. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73 m^2. For more information, please see the American College of Radiology (ACR) Manual on Contrast Media (see the "Availability of Companion Documents" field).

Relative Radiation Level (RRL)

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

Contraindications

Contraindications

- Surgery is contraindicated by local extension if the brachial plexus is involved above the level of T1, if more than 50% of a vertebral body is invaded, or if there is invasion of the trachea or esophagus.
- Invasion of the subclavian, common carotid and vertebral arteries, less than 50% vertebral body invasion, and extension into the neural foramina should be considered relative contraindications to surgery.

Qualifying Statements

Qualifying Statements

The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report

Categories

IOM Care Need

End of Life Care

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Ravenel JG, Mohammed TH, Rosenzweig KE, Ginsburg ME, Kanne JP, Kestin LL, Kirsch J, Parker JA, Rimner A, Saleh AG, Expert Panels on Thoracic Imaging and Radiation Oncologyâ€“Lung. ACR Appropriateness CriteriaÂ® non-invasive clinical staging of bronchogenic carcinoma. [online publication]. Reston (VA): American College of Radiology (ACR); 2013. 11 p. [68 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1995 (revised 2013)

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panels on Thoracic Imaging and Radiation Oncology–Lung

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Ravenel JG, Mohammed TH, Movsas B, Ginsburg ME, Kirsch J, Kong FM, Parker JA, Reddy GP, Rosenzweig KE, Saleh AG, Expert Panel on Thoracic Imaging and Radiation-Oncology-Lung. ACR Appropriateness Criteria® non-invasive clinical staging of bronchogenic carcinoma. [online publication]. Reston (VA): American College of Radiology (ACR); 2010. 11 p.

Guideline Availability

Electronic copies: Available from the American College of Radiology (ACR) Web site .

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site .
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2013 Apr. 1 p. Electronic copies: Available in PDF from the ACR Web site .
- ACR Appropriateness Criteria®. Evidence table development – diagnostic studies. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available in PDF from the ACR Web site .
- ACR Appropriateness Criteria®. Evidence table development – therapeutic studies. Reston (VA): American College of Radiology; 2013 Nov. 4 p. Electronic copies: Available in PDF from the ACR Web site .
- ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2013 Nov. 3 p. Electronic copies: Available in PDF from the ACR Web site .
- ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 90 p. Electronic copies: Available in PDF from the ACR Web site .
- ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 2013 Apr. 1 p. Electronic copies: Available in PDF from the ACR Web site .
- ACR Appropriateness Criteria® non-invasive clinical staging of bronchogenic carcinoma. Evidence table. Reston (VA): American College of Radiology; 2013. 31 p. Electronic copies: Available from the ACR Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on March 6, 2006. This NGC summary was updated by ECRI Institute on July 31, 2009. This summary was updated by ECRI Institute on January 13, 2011 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This NGC summary was updated by ECRI Institute on July 27, 2011. This NGC summary was updated by ECRI Institute on March 7, 2014.

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